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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/981,289	DAHIYAT ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/25/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/25/2004 has been entered. An action on the RCE follows.

2. Claims 1-3 and 16-27 have been cancelled. Claims 29-49 have been added. Therefore, Claims are 28-49 are pending.

3. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

4. The pending rejections of claims 1-3 and 13-27 are withdrawn because Applicant has elected to cancel these pending claims. However, any remarks related to the newly added claims will be addressed below as it applies to claims 28-49.

5. New claim rejections necessitated by Applicants amendments.

Claim Rejections - 35 USC § 112

6. Claims 28-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6a. Claim 28 is rejected as vague and indefinite because it is unclear as to what receptor if any signaling activation is affected by mixed trimers of TNF.

6b. Claims 29-45 are rejected as vague and indefinite because the claims call for one or more amino acid substitution compared to naturally occurring human TNF. However, more than one amino acid change is not defined. It could potentially include amino acid changes that include the functional motifs or entire TNF polypeptide and not resemble the TNF functionally or structurally. Therefore, metes and bounds can't be determined. Claims 30-35, 37-39, 41-42 and 44-45 and 47-49 are rejected insofar as they depend on claims 29, 36, 40 and 43.

6c. Claims 29-49 are rejected as vague and indefinite because the claims call for at least one amino acid substitution but do not require any conservation of structure or function. Therefore, metes and bounds can't be determined. Claims 30-35, 37-39, 41-42, 44-45 and 47-49 are rejected insofar as they depend on claims 29, 36, 40, 43 and 46.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7a. Claims 37, 46-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a new matter rejection.*

The newly introduced claims contain several amino acid substitutions (ex: Q21K, N30E, R31V, R31L, R32H, R32T, A35T, G66N, G66R, G66E, A111K, A111D, Y115V, D140Q, D140E, F144Q, F144H, E146D, E146Q, E146H, E146E, E146T and A84V) that were not originally described. Although, Applicant asserts that there is support for these substitutions in the specification and claims as originally filed, the Office cannot find support these substitutions in the specification including Figure 7.

7b. Claim 28 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses the nucleotides encoding a human TNF-α (SEQ ID NO: 2) and substitutions at wild-type positions 21, 30, 31, 32, 33, 35, 65, 66, 67, 111, 112, 115, 140 and 143 (Figure: 7). This meets the written description and enablement provisions of 35 USC 112, first paragraph. However, the specification does not disclose all variant TNF-α sequences with one or more amino acid substitution. Absent a comparison sequence, additional variants encompassed have not been set forth in the instant specification. The claim as written, however, encompass variant TNF-α sequences which were not originally described and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claim 28. In the instant claims non-

naturally occurring variant sequence is compared to a naturally occurring human TNF-α. There is no description of all naturally occurring human TNF-α. This is due to the fact that the allelic variant sequence is an alternative form of the gene that may result from at least one mutation in the nucleic acid sequence. Alleles may result in altered mRNAs or polypeptides whose structure or function may or may not be altered. Any given gene may have none, one, or many allelic forms. Common mutational changes, which give rise to alleles, are generally ascribed to natural deletions, additions, or substitutions of nucleotides. However, claim recites at least one amino acid substitution in the TNF-α polypeptide. Thus, the specification does not provide written description to support the genus encompassed by the instant claims. In addition, specification fails to describe the maximum number of possible changes to the human TNF-α and yet retain the TNF-α activity.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (*See Vas-Cath* at page 1116).

With the exception of isolated polynucleotide encoding the TNF-α polypeptide of SEQ ID NO: 2 comprising substitutions at wild-type positions 21, 30, 31, 32, 33, 35, 65, 66, 67, 111, 112, 115, 140 and 143, the skilled artisan cannot envision all the detailed chemical structure of the claimed nucleotide sequences of the variants, regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide

itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only the isolated polynucleotide encoding the TNF-α polypeptide of SEQ ID NO: 2 with substitutions at wild-type positions 21, 30, 31, 32, 33, 35, 65, 66, 67, 84, 111, 112, 115, 140 and 143, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. As a result, it does not appear that the inventors were in possession of various polypeptide sequences set forth in claim 28.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

7c. Claims 29-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses the nucleotides encoding a human TNF-α (SEQ ID NO: 2) and substitutions at wild-type positions 21, 30, 31, 32, 33, 35, 65, 66, 67, 111, 112, 115, 140, 143, 144, 145, 146 and 147 (Figure: 7). Also described are the double mutants K65E/D143K, K65E/D143R, K65D/D143K and K65D/143R. The specification also discloses changes at positions K112D, Y115T, D143K, D143R and Y115I. Further, it is asserted that these changes maybe may be done either individually or in combination, with any combination being possible (paragraph 0139). This meets the written description and enablement provisions of 35 USC 112, first paragraph. Preferred embodiments are asserted to utilize at least 1 to 5 changes, and preferably more, positions in each variant TNF-α. However, the specification does not disclose all variant TNF-α sequences with one or more amino acid substitution. The claims as written, however, encompass variant TNF-α sequences which were not originally described and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claims 29-45.

Although, Applicant asserts in their response of 6/25/2004, that the specification recites more than 70 variant TNF-α proteins, none of these mutations contain more than 2 amino acid changes. However, claims recite one or more amino acid substitution in the TNF-α polypeptide. Thus, the specification does not provide written description to support the genus encompassed by the instant claims. In addition, specification fails to describe the maximum number of possible changes to the human TNF-α and yet retain the TNF-α activity.

With the exception of isolated polynucleotide encoding the TNF-α polypeptide of SEQ ID NO: 2 with substitutions at wild-type positions 21, 30, 31, 32, 33, 35, 65, 66, 67, 111, 112, 115, 140, 143, 144, 145, 146, 147 the double mutant of 65/143 and changes at 112, 115 and 143 alone or in combination, the skilled artisan cannot envision all the detailed chemical structure of the claimed nucleotide sequences of the variants, regardless of the complexity or simplicity of the method of isolation.

Therefore, only the isolated polynucleotide encoding the TNF-α polypeptide of SEQ ID NO: 2 with substitutions at wild-type positions 21, 30, 31, 32, 33, 35, 65, 66, 67, 84, 111, 112, 115, 140, 143, 144, 145, 146, 147, the double mutant of 65/143 and changes at 112, 115 and 143 alone or in combination, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. As a result, it does not appear that the inventors were in possession of the entire genus encompassing the various polypeptide sequences encompassed within claims 29-45.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

7d. Claims 29-37 and 40-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for polynucleotides encoding TNF-α variants at positions K112D, Y115T, D143K, D143R, Y115I, D143E, A145R, A145K, A145E, E146K and E146R with respect to wild-type TNF-α of SEQ ID NO: 2 activities as described in Figures 8, 9, 10a and 10b does not reasonably provide enablement for all non-naturally occurring variants of TNF-α. Applicants in their response filed on 6/25/2004 correctly point out that the specification provides experimental data for 11 variant TNF-α sequences. However, this data only demonstrates the activity of single amino acid substitution on TNF-α sequence and does not demonstrate multiple amino acid substitutions. Further. Applicant contends that the antigenic profile of the variant proteins should be similar to the wild-type protein. This will only be true provided that there is no significant altering of surface residues. In addition, since only about six residues are required to generate an antigenic epitope, as long there are six contiguous residues that are similar in both the wild-type protein and the variant the antigenic profile will be the same. Specifically, the specification fails to demonstrate any activity with more than one amino acid substitution as compared to wild type human TNF-α of SEQ ID NO: 2. Thus, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is

sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Despite knowledge in the art for producing non-naturally occurring variants of a given polypeptide with amino acid deletions, insertions or substitutions the specification fails to provide any guidance regarding the changes/modifications contemplated and yet retain the function of the TNF-α variants claimed. Furthermore, detailed information regarding the structural and functional requirements of the disclosed protein is lacking. Although it is accepted that the amino acid sequence of a polypeptide determines its structural and functional properties, predicting a protein's structure and function from mere sequence data remains an elusive task. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-

dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495, previously submitted with the Office Action of 10/22/2002). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Applicant has failed to demonstrate any activity with more than one amino acid substitution as compared to wild type human TNF-α of SEQ ID NO: 2.

Although the specification outlines art-recognized procedures for producing and screening for active variants, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. There is no description of the activity contemplated by the changes contemplated by the Applicant. Therefore, predicting which nucleotide

sequence encoding the non-naturally occurring variants would retain the functions of the TNF-α protein is well outside the realm of routine experimentation. Thus, undue amount of experimentation would be required to generate changes/modifications of the nucleotides contemplated and yet retain the function of the non-naturally occurring variant TNF-α proteins claimed.

Applicants have not taught how one of skill in the art would use the invention in a manner commensurate in scope with the polynucleotide sequences encompassed by the invention of claims 28-37 and 40-49. The specification as filed does not sufficiently teach one of skill in the art how to make and/or use the full scope of the claimed sequences. The amount of experimentation required to make and/or use the claimed sequences would require trial and error experimentation to determine the functional sequences. Given the breadth of claims 28-37 and 40-49 in light of the unpredictability of the art as determined by the lack of working examples and shown by the prior at of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

7e. Claims 28 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for various activities described in Figures 8, 9, 10a and 10b, is not enabling for the activation of receptor signaling. Without guidance as to how to test for activation receptor signaling, one of skill in the art would not know how to use the instant invention.

Claim Rejections - 35 USC § 102

8. Claims 28-37, 46, 48 and 49 remain rejected under 35 USC § 102(b) as being anticipated by Banner et al. (U.S. Patent NO: 5, 597, 899) and as evidenced by Shin et al. (U.S. Patent No. 5, 773, 582), for reasons set forth in Paper Nos: 13, 18 and 21.

As stated previously, the Office relied on the Banner reference to teach the generation of the various TNF-alpha mutations with at least one amino acid substitution. This reference teaches the preparation of mutations at several different amino acid positions compared to the wild-type TNF-α, which has different binding affinity to p55-TNF receptor compared to p75 TNF receptor. Using standard molecular biology techniques (abstract). Amino acid substitutions have been made at 33, 34, 65, 67, 75, 143, 145 and 147, including the following changes: D143N, D143E, A145R and A145K (abstract and Tables I and II). It also teaches generation of multiple amino acid substitutions compared to wild-type TNF-α sequence, including at least 3 amino acid substitutions (columns 5 and 6). Although Banner et al. may not have appreciated the trimer formation itself nonetheless meets the limitations of the instant claims in the teaching of the generation of various amino acid mutations. As noted previously in the Office Action of 12/23/2003 the following evidentiary art of Shin et al. (U.S. Patent No. 5, 773, 582), human TNF -α is known to exist as a trimer with 3-fold axis of symmetry (column 1, lines 64-67). Further the formation of mixed trimers is a consequence of generating the TNF mutants described in the prior art because it is necessary to at least have two different forms of TNF -α to generate the mixed trimers. Despite the fact that applicants may have been the first to characterize the formation of mixed trimers, the

formation of mixed trimers would inherently have occurred in the presence of the teachings of Bennett et al. mutants, which are similar to those of the instant invention. The mixed trimers will comprise either a single TNF mutein monomer or two TNF mutein monomers or three TNF mutein monomers in combination with the naturally occurring TNF monomer. In addition, these mutein monomers could be identical or different. Therefore, Banner et al. anticipates variants that are capable of forming mixed trimers, exchange with naturally occurring human- TNF -α and/or inactivate receptor signaling because this activity is inherent to TNF receptors. Although, the Banner reference teaches muteins with higher binding affinity and greater specificity for hp75-TNF-R (column 3, lines1-5), it is silent on receptor signaling. Therefore, there is no teaching away from the instant invention. In addition, Banner et al. also teaches covalent modification of the muteins using polyethylene glycol (column 8, lines 5-18).

The Examiner also notes the decision in *Swinehart and Sfiligoj*, 169 USPQ 226, in which it was found that mere recitation of a newly discovered function or property, inherently possessed by things in prior art, does not cause claim drawn to those things to distinguish over prior art. Although the prior art did not necessarily appreciate the mechanism of the formation of the mixed trimers comprising the TNF muteins, it clearly teaches the same TNF-alpha mutants which are capable of forming the mixed trimers of the instant invention. Thus, claims 28-37, 46, 48 and 49 remain rejected under 35 USC § 102 (b) as being anticipated by Banner et al. (U.S. Patent NO: 5, 597, 899).

Claim Rejections - 35 USC § 103

9. Claims 40-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banner et al. (U.S. Patent NO: 5, 597, 899) in view of Wallach et al. (U.S. Patent NO: 5, 695, 953).

The instant invention is drawn to glycosylated TNF -α muteins.

The teachings of Banner et al. (U.S. Patent NO: 5, 597, 899) has been described above in paragraph 8. However, Banner et al. do not describe glycosylated TNF -α muteins. Wallach et al. (U.S. Patent NO: 5, 695, 953) describe that proteins expressed in mammalian cells such as human and CHO cells provide post-translational modifications to protein including glycosylation (column 15, lines 24-28). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to express the muteins disclosed in Banner et al. to generate the various glycosylated TNF muteins of the instant invention as described by Wallach et al. One of ordinary skill would have been motivated with reasonable expectation of success to

generate muteins of Banner et al. that are glycsylated because variants of TNF-α generated, form mixed trimers that make the TNF incapable of activating receptor signaling or alter the biological activity of the mixed trimers. Therefore, the instant invention is prima facie obvious over Banner et al. (U.S. Patent NO: 5, 597, 899) in view of Wallach et al. (U.S. Patent NO: 5, 695, 953).

10. Applicant is advised that should claim 33 be found allowable, claim 34 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

11. Claims 38, 39 and 47-49 if written independent of claim 36 and 46 will be allowable over prior art. Claims 28-37 and 40-45 are not allowable over prior art.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS 09/04

Brenda Brumback

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